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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/687,373	10/16/2003	James M. Chen	263.PC2	9295

25000 7590 07/21/2006

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EXAMINER	
RAHMANI, NILOOFAR	

ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 07/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/687,373	CHEN ET AL.	
	Examiner	Art Unit	
	Niloofar Rahmani	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-55,58,63-70 and 80-89* is/are pending in the application.

4a) Of the above claim(s) *64-70, and 81-89* is/are withdrawn from consideration.

5)☒ Claim(s) *53* is/are allowed.

6)☒ Claim(s) *1-52,54,55,58,63 and 80* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Amendment and response filed by applicant's date 06/19/2006 has been entered and considered carefully. Claims 1-55,58,63-70,80-89 are pending. Claims 64-70, and 81-89 are withdrawn, see paper dated 06/24/2004. Claims 56-57, 59-62, and 71-79 are cancelled.

Priority

2. This application is file on 10/16/2003, which claims benefit of 60/418,963, filed on 10/16/2002 and claims benefit of 60/478,783, filed on 06/16/2003.

3. The rejection of claims 22, 45, 48 under 35 U.S.C. 101 over the claims 22, 45, 48 of copending application # 10/687,374 is withdrawn. Since the application 10/687,374 has gone abandoned.

4. The rejection of claims 1-21, 23-44, 46-47, 49-63, 68, and 80 under 35 U.S.C. 101 for Obvious Double Patenting over the claims 1-21, 23-44, 46-47, 49-63 of copending application # 10/687,374 is withdrawn. Since the application 10/687,374 has gone abandoned.

5. The rejection of claims 1-44, 46, 49-52, 54-55, 63, and 80 under 35 U.S.C. 112, second paragraph for " Ar" is withdrawn in view of the applicant's amendment.

6. The rejection of claim 49 for " P" under 35 U.S.C. 112, first paragraph is maintained for reason of record. Applicant argues that the definition for the term "P" in claim 49 as amended can be found in claim 49 as originally filed. It is the examiner's position that the specification does not have the definition for the term

"P". However, originally filed claims have the definition for the term "P". The definition of "P" can be put in to the specification to fix this problem as long as the definition is limited to the definition from originally filed claim 49.

7. *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 49 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter that was not described in the specification in such a way to convey reasonably to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The specification lacks description of the claims i.e. "P". There is no description for P as a protecting group selected from R_3Si and CH_2OR and C(=O)R while R being phosphate, C_2-C_{20} heteroaryl, phosphonate, polyethyleneoxy, aryl other than alky. Therefore, the specification lacks description of "P".

8. *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-44, 46, 50-52, 54-55, 58, 63, and 80 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making salts of the claimed compounds, does not reasonably provide enablement for making prodrugs of the claimed compounds. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art of medicinal chemistry to use the invention. "The factors to be considered [in making an enablement rejection] have been summarized as a) the quantity of experimentation necessary, b) the amount of direction or guidance presented, c) the presence or absence of working examples, d) the nature of the invention, e) the state of the prior art, f) the relative skill of those in that art, g) the predictability or unpredictability of the art, h) and the breadth of the claims", *In re Rainer*, 146 USPQ 218 (1965); *In re Colianni*, 195 USPQ 150, *Ex parte Formal*, 230 USPQ 546. a) Finding a prodrug is an empirical exercise. Predicting if a certain ester of a claimed alcohol, for example, is in fact a prodrug, that produces the active compound metabolically, in man, at a therapeutic concentration and at a useful rate is filled with experimental uncertainty. Although attempts have been made to predict drug metabolism *de novo*, this is still an experimental science. For a compound to be a prodrug, it must meet three tests. It must itself be biologically inactive. It must be metabolized to a second substance in a human at a rate and to an extent to produce that second substance at a physiologically meaningful concentration. Thirdly, that second substance must be clinically effective. Determining whether

a particular compound meets these three criteria in a clinical trial setting requires a large quantity of experimentation.

b) The direction concerning the prodrugs is found in the specification, on page 7-8. c) There is no working example of a prodrug of a compound the formula in claim 1. d) The nature of the invention is clinical use of compounds and the pharmacokinetic behavior of substances in the human body. e) Wolff (Medicinal Chemistry) summarizes the state of the prodrug art. Wolff, Manfred E. "Burger's Medicinal Chemistry, 5ed, Part I", John Wiley & Sons, 1995, pages 975-977. The table on the left side of page 976 outlines the research program to be undertaken to find a prodrug. The second paragraph in section 10 and the paragraph spanning pages 976-977 indicate the low expectation of success. In that paragraph the difficulties of extrapolating between species are further developed. Since, the prodrug concept is a pharmacokinetic issue, the lack of any standard pharmacokinetic protocol discussed in the last sentence of this paragraph is particularly relevant. Banker (Modern Pharmaceutics) Banker, G.S. et al, "Modern Pharmaceutics, 3ed.", Marcel Dekker, New York, 1996, pages 451 and 596. in the first sentence, third paragraph on page 596 states that "extensive development must be undertaken" to find a prodrug. f) Wolff (Medicinal Chemistry) in the last paragraph on page 975 describes the artisans making Applicants' prodrugs as a collaborative team of synthetic pharmaceutical chemists and metabolism experts. All would have a Ph. D. degree and several years of industrial experience. g) It is well established that "the scope of

enablement varies inversely with the degree of unpredictability of the factors involved", and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). h) The breadth of the claims includes all of the hundreds of thousands of compounds of formula of claim 1 as well as the presently unknown list of potential prodrug derivatives embraced by claim 1.

9. *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term " protecting group" is undefined. The protecting group should be specified in the claims. There are many protecting groups available out there.

10. *Claim Rejections - Obvious Double Patenting*

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 168 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130 (b).

Effective January 1,1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-49, 54-55, 58 and 80 are provisionally rejected under the judicially created doctrine obviousness-type double patenting as being unpatentable over claim 24 of US 2006/0116356 (ap# 11/106,363). Although the conflicting claims are not identical, they are not patentably distinct from each other because the current invention embraces the invention claimed in the above conflicting application based on the ground of the overlapping relationship.

Determination of the scope and content of the prior art (MPEP §2141.01)

Cai et al. of US 2006/0116356 claimed claim 24,which is an HIV ingrase inhibitor compound of formula I analogues to the instant claims 1-49, 54-55,58 and 80.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the instant claims and the prior art claim is that the prior art claim has more broader definition for A^4 and A^5 which are corresponded to A^1 and A^2 in the instant claims.

Finding of prima facia obviousness-rational and motivation (MPEP §2142.2143)

The instant claims 1-49, 54-55, 58 and 80 are therefore fully embraced by the prior art claim 24.

This is provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

11. *Allowable Subject Matter*

Claim 53 is patentable over Murray et al., Synthesis, Vol. 10, pages 1180-1182. The reference teaches L being bond instead of the CH_2 in the instant claim. Therefore, the claims are free of prior art.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Niloofar Rahmani whose telephone number is 571-272-4329. The examiner can normally be reached on Monday through Friday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thomas Mckenzie, can be reached on 571-272-0670. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

NILOOFAR RAHMANI
07/13/2006
NR

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